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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,797	12/04/2001	John David Fraser	12669-002001/30072UPS00	9884

26161 7590 09/07/2005

FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,797	FRASER ET AL.	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 12/04/01, is acknowledged. Claims pending: 1-18, 21-38.

2. Applicant's election without traverse of group I, claims 1-16, in the reply filed on 12/9/04 is acknowledged. Furthermore, applicant has elected the species of SPEC as the species to be examined first. Therefore, Claims 17-18 and 21-38 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 5, 7-9, and 14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

Claims 1-4, 6, 10-13, and 15-16 read on the elected invention and are being acted upon.

3. The amendment of 4/5/02 is objected to. A marked-up copy of the amendment is required.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4, 6, 10-13, and 15-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The terms "immunomodulator" and "immunomodulatory" in claims 1-2 are indefinite because it is ambiguous as the direction (positive or negative) or degree of said immunomodulator. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. As claims 3-4, 6, 10-13, and 15-16 depend on claim 1, and do not clarify the indefiniteness of the invention, they are also rejected.

B) Additionally, the terms "fully functional" in Claim 1 and "little or no ability" in Claim 2 are relative terms which render the claims indefinite. The terms are not defined by the claim or the specification, the specification does not provide a

standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. The recitation "little" as pertaining to ability of a superantigen to activate T cells is vague. It is known that disruption of superantigen T cell receptor binding sites can result in reduced ability to stimulate only certain subsets of T cells, while being fully functional to stimulate other subsets (see Kappler et al., p391, paragraph 4). It is unclear whether a superantigen with such a disruption might reasonably be considered to have a "little" ability to activate T cells. Furthermore, disruption of the T cell receptor binding site may result in a wide range of effects on the ability of a superantigen to stimulate T cells (see Kappler et al. Fig. 4-6). For example, a disruption that results in a 10,000 fold reduction in T cell stimulatory capacity (as disclosed for SMEZ-2 D42N of the instant application) would be considered to have "little" ability to activate T cells. However, it is not defined by the claim or the specification if a modification that resulted in, for example, only a 2 fold reduction might also be considered to have "little" ability to activate T cells. Furthermore, the recitation of "fully functional T cell receptor binding site" in Claim 1 is indefinite. Since a superantigen can bind T cells and/or stimulate T cells, it is unclear if the term "functional" relates to either or both of those functions. Likewise, the term "fully" is vague. It is not clear what degree of impairment is necessary to be considered not fully functional. Therefore, the claims as written do not define the metes and bounds of the invention. As claims 6, 10-13, and 15-16 depend on claim 1, and do not clarify the indefiniteness of the invention, they are also rejected.

C) Additionally, the term "non-immunogenic" in Claim 13, as pertaining to an immunomodulatory antigen is indefinite. It is unclear how an antigen can be both immunomodulatory (i.e. capable of positively or negatively stimulating an immune response) and also non-immunogenic (i.e. not capable of stimulating an immune response.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and

use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1–4, 11-13, and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, Applicant has not adequately disclosed that they are in possession of APC-targeting molecules that "mimic" a superantigen or that are "structurally" a superantigen.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

In the instant case, Applicant is in possession of specific APC targeting molecules that are mutated superantigens, as disclosed in Table 2 of the instant specification. However, Applicant has not adequately disclosed that they are in possession of APC-targeting molecules that "mimic" a superantigen or that are "structurally" a superantigen. For example, an antibody which is specific for MHC-II could be considered a mimic of a superantigen or structurally a superantigen (i.e. binds to MHC-II, and contains an MHC-II binding region). Thus, Applicant has only disclosed a limited number of APC targeting molecules. It does not appear based upon the limited disclosure that Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the limited

number of species disclosed and the extensive variation permitted within the genus of "mimics a superantigen" or "structurally a superantigen."

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the material does, rather than of what it is, does not suffice.

8. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification does not adequately enable one skilled in the art to make or use an APC targeting molecule coupled to a nucleic acid.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The instant specification does not adequately enable one skilled in the art to make or use an APC targeting molecule coupled to a nucleic acid. Applicant has gone to great length to disclose methods of coupling APC-targeting molecules to proteins or peptides (pg. 21, 26), however, nothing in the specification or examples enables one of ordinary skill in the

art to couple an APC targeting molecule to a nucleic acid. Additionally, the specification fails to provide guidance for how to use an APC targeting molecule coupled to a nucleic acid as an immunomodulator. It appears that said nucleic acid would be required to be delivered to the nucleus, and transcribed and translated into a protein in order to modulate an immune response. It is known in the art that the delivery and expression of nucleic acids into cells is unpredictable and influenced by many factors, such as the type of vector used for delivery, the half life of said vector in vivo, the type of nucleic acid being expressed, and the efficacy of transcription/translation of the nucleic acid after delivery (see Goncalves et. al). In the instant case, the specification is silent as to the type of nucleic acid to be used, its half-life and availability in vivo, how it would be delivered to the nucleus, and how it would be transcribed and translated into a protein. Thus, given the unpredictability of the art and the lack of guidance in the instant specification, one of ordinary skill in the art is not enabled to make or use the invention as claimed.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 10-11, and 15-16, are rejected under 35 U.S.C. 102(b) as being anticipated by Yamoaoka e al, 1998, Infection and Immunity, vol. 66 pp. 5020-5026.

Yamaoka teaches a mutated superantigen that has a disrupted/non-fully functional T cell receptor binding site (see materials and methods). Said mutated superantigen is coupled to an antigen (GST, see pg 5022 paragraph 1) and can act as an immunomodulator, in that it can weakly stimulate peripheral blood lymphocytes (see fig. 2). Furthermore, said mutated superantigen is derived from SPE-C, (see pg. 5020, materials and methods). Claim 3 is included since the superantigen was mutated by amino acid substitution. Claim 4 is included since the T cell receptor binding site of the superantigen has been deleted (i.e. is non-functional and therefore not present). Claim 10 and 11 are included since Yamaoka teaches that the superantigen is reversibly coupled to a protein (GST can be

cleaved off - see pp. 5022 paragraph 1). Claims 15-16 have been included since the reference teaches using the mutated superantigen in vivo (i.e. as a pharmaceutical composition or vaccine - see fig. 2, and pg. 5023).

The reference clearly anticipates the invention.

10. No claim is allowed. Claims 12-13 are free of the art.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy E. Juedes, Ph.D.
Patent Examiner
Technology Center 1600
August 22, 2005

9/1/05
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER